A Dissertation on

"COMPARATIVE EVALUATION OF LOW DOSE INTRATHECAL MORPHINE VS MULTIMODAL ANALGESIA IN PATIENTS UNDERGOING ABDOMINAL SURGERIES UNDER GENERAL ANAESTHESIA"

Dissertation Submitted in partial fulfillment of

M.D. DEGREE EXAMINATION
BRANCH X - ANAESTHESIOLOGY
MADRAS MEDICAL COLLEGE, CHENNAI

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY
CHENNAI, TAMILNADU

MARCH 2009

CERTIFICATE

This is to certify that the dissertation **"Comparative Evaluation of Low dose intrathecal Morphine Vs Multimodal analgesia in Patients undergoing abdominal surgeries under general anaesthesia"** presented herein by Dr.B.Jayasankara Narayanan, is an original work done in the Department of Anaesthesiology, Madras Medical College for the award of Degree of M.D. (Branch X) Anaesthesiology under my guidance and supervision during the academic period 2006 - 2009

Prof. Dr. T.P.Kalanithi M.D,
Dean
Madras Medical College and
Government General Hospital
Chennai – 600 003.

Prof. Dr.Kamalini Sridharan, M.D, D.A.,
Professor and Head
Department of Anesthesiology,
Madras Medical College and
Government General Hospital
Chennai – 600 003.

Place : Chennai-3
Date :

DECLARATION

I hereby declare that dissertation entitled **"Comparative Evaluation of Low dose intrathecal Morphine Vs Multimodal analgesia in Patients undergoing abdominal surgeries under general anaesthesia"** has been prepared by me under the guidance of Prof. Dr.Kamalini Sridharan, M.D. D.A. Professor and Head of the Department of Anaesthesiology, Madras Medical College, Chennai in partial fulfillment of the regulations for the award of the degree of M.D. (Anaesthesiology), examination to be held in March 2009.

This study was conducted at Madras Medical College and Government General Hospital, Chennai.

I have not submitted this dissertation previously to any university for the award of any degree or diploma.

Date :

Place : Chennai **Dr.B.Jayasankara Narayanan**

ACKNOWLEDGEMENT

I am greatly indebted to Dr.T.P.Kalanithi, M.D., Dean, Madras Medical College and Government General Hospital, Chennai - 600 003, for allowing me to use the facilities of the hospital to conduct this study.

I express my deep sense of gratitude to Prof. Dr.Kamalini Sridharan, M.D, D.A.,Professor and Head of the Department of Anesthesiology, Madras Medical College, Chennai for her constant encouragement and invaluable guidance.

My sincere thanks of Prof. Dr.C.R.Kanyakumari, M.D., D.A., for her constant supervision and encouragement to do this study.

My sincere thanks of Prof. Dr.Esther Sudharshini Rajkumar, M.D., D.A., for her constant supervision and encouragement to do this study.

My sincere thanks to Prof. Dr.T.Venkatachalam, M.D., D.A., for his continuously supervision and able guidance throughout this work.

My sincere thanks to Prof. Dr.D.Kandhimathi, M.D., D.A. for her encouragement and guidance throughout this work.

I express my heart felt gratitude to my guide Dr.A.Chandrasekar, M.D., D.A. Assistant Professor, for constant guidance and help in every step of this study.

I thank all the Assistant Professors and tutors of anaesthesiology for their able help and support during the course of study.

I thank all the professors of surgery and surgical units chiefs and Assistant Professors of surgery to do study on their Patients.

I also express my thanks to all my colleagues for their co-operation and support for this study.

I express my heartfelt gratitude to Mr.Asaithambi, M.Sc., statistician (Retd.) Indian council of Medical Research, Madurai Medical College, Madurai for his guidance and expert advice in the statistical analysis of the study data.

I thank all the patients included in the study and their relatives, for main whole hearted co-operation inspite their illness.

My sincere thanks to all the staff nurses and theatre personnel for their help for this study.

I wish to express my thanks to my family and friends for their moral support and encouragement.

Last but not the least, I would like to express my sincere gratitude to Lord Almighty.

CONTENTS

INTRODUCTION

Opioids have been used in the treatment of pain for thousands of years. The opioids contains 20 alkaloids. Opium means juice, from Greek word. Morphine is the prototype drug and named after Greek God of dreams, Morpheous.

Morphine was used in American civil war in 1869. In 1950. Opioid anesthesia came with advent of cardiac surgery. However, because of incomplete suppression of stress response, hypotension, awareness during anesthesia and increased fluid and blood requirement and need to ventilate post operatively, limited its use.

Opioid refers to drugs derived from opium both natural and synthetic. Narcotic refers to morphine and morphine-like analgesics.

Morphine can be used as spinal analgesic, Epidural analgesic as shown by Behar et al. Despite the high efficacy, it was not widely used because of early reported high incidence of respiratory depression and somnolence. It was due to high doses, rather than route of administration.

Gwirtz and associates recently reported high patient satisfaction and low incidence of side effects and complication of morphine over 6000 patients.

Therefore, this study has been undertaken to analyze the effect of intrathecal morphine as more cost effective analgesic when compared to Multimodal analgesia.

AIM OF STUDY

To evaluate the effect of preservative free morphine 0.5 mg administered intrathecally, on intraoperative anaesthetic requirement and postoperative analgesia in patients undergoing laparotomies under general anesthesia compared with multimodal analgesia, during the Ist 24 hours of postoperative period.

The following parameters were studied

1. Intra operative hemodynamics
2. Post operative pain score and analgesic requirement
3. Post operative hemodynamics
4. Complications: both intraoperative and postoperative period

SPINAL ANAESTHESIA

Spinal anesthesia is a form of central neuraxial block in which a temporary interruption of impulse transmission is achieved following injection of local anaesthetic and or adjuvant solutions into the subarachnoid space.

Spinal anaesthesia is one of the most frequently employed methods of regional anaesthesia.

Anatomy

The vertebral canal extends from the foramen magnum to the sacral hiatus. It is formed dorsal spine, pedicles and laminae of successive vertebra (7 cervical, 12 thoracic, 5 Lumbar and 5 sacral). The vertebral are held together by a series of overlapping ligaments, ligamentum flavum, interspinous ligament, supraspinous ligament and the intervertebral disc.

The spinal cord, a direct continuation of the medulla oblongata begins at the upper border of the atlas and terminates distally in the conus medullaris. The distal termination, because of the differential growth rates between the bony vertebral canal and central nervous system varies from L3 in the infant, to the lower border of L1 in the Adult.

Surrounding the spinal cord in the bony vertebral column are three membranes (from within to the periphery) the piamater, arachnoidmater and duramater. The piamater is highly vascular membrane that closely invests the spinal cord. The arachnoidmater is a delicate non-vascular membrane closely attached to the outer most duramater.

Between the two inner most membranes is the subarachnoid space. In this space are the cerebrospinal fluid (CSF), spinal nerves, blood vessels that supply the spinal cord and the dentate ligaments. Although the spinal cord ends at the lower border of L_1 in adults, the subarachnoid space continues up to S_2. The outer membrane in the spinal canal is the longitudinally organized fibroelastic membrane, the duramater. This layer is the direct extension of the cranial duramater and extends as spinal duramater from the foramen magnum to S_2, where the filum terminale (an extension of the piamater beginning at the conus medullaris) blends with the periosteum of the coccyx. There is a potential space between the duramater and arachnoid, the subdural space, which contains only small amount of serous fluid to allow the dura and arachnoid move over each other. Surrounding the duramater is epidural space, which extends from the foramen magnum to the sacral hiatus. Immediately posterior to ligamentum flavum is the interspinous ligament, extending from the external occipital protuberance to the coccyx, posterior to these structures is the supraspinous ligament.

Lumbar puncture is routinely done below the L_2 vertebra down to the L_5 - S_1 interspace to avoid damaging the spinal cord that ends at the lower border of L_1 vertebra in adults.

PHYSIOLOGY OF SUBARACHNOID BLOCK

Cerebrospinal Fluid

The cerebrospinal fluid is an ultra filtrate of blood and plasma with which, it is in hydrostatic and osmotic equilibrium. It is clear, colourless fluid found in the spinal and cranial subarachnoid space and in the ventricles of the brain. The average volume in the adult ranges from 120 - 150 ml, of which 35 ml is in the ventricles, 25 ml is in the cerebral subarachnoid space and 75 ml is in the spinal subarachnoid space. It is secreted by the choroid plexus of lateral ventricles at a rate of 0.3 - 0.4 ml/minute.

Physical characteristics of Cerebrospinal Fluid

pH	7.4
Specific gravity	referred to H_2O
at body temperature	1.007
at 4°C	1.0003
Density	1.0003 g/ml
Baricity	1.000
Pressure	8 - 12 mm Hg / 70-80 mm H_2O
Cells	3-5 / cu.mm
Proteins	20 mg / dl
Glucose	45 - 80 mg/dl

The Cerebrospinal fluid plays an important role in spinal anesthesia as media for dispersion of the local anesthetic drug to the spinal nerve. An

important factor determining the spread of drugs in the subarachnoid space is the specific gravity of the injected solution compared to that of C.S.F.

In our study preservative free morphine is diluted with 0.9% Nacl and injected intrathecally, which is isobaric to C.S.F. The morphine injected intrathecally is diluted by C.S.F and there for original concentration is of less important than the actual mass of drug. Spread is also determined by the baricity of the injected solution.

Baricity is a ratio comparing the density of any solution(morphine) at specified temperature to the density of CSF at the same temperature.

Contraindications for subarachnoid block

An absolute contraindication is patient refusal.

Other contraindications are

Local sepsis

Uncorrected coagulopathy

Uncontrolled blood loss / shock

Fixed cardiac output states

Documented allergy to study drug (Morphine, if any)

Raised intracranial pressure

Active neurological disease

Major spine deformities / previous surgery on the spine

Severe cardiac disease

Subarachnoid block technique

First step in the successful conduct of spinal anesthesia is proper patient selection. This is accomplished by preanesthetic evaluation of the patient through history, physical examination, laboratory data and communication with the patient and surgical colleagues about details of the procedure. Premedication is Tab. Alprazolam 0.25 mg and Ranitidine 150mg P.O., 2 hours before surgery is given.

Patient is explained the procedure previous day and visual analog score is also explained to him preoperatively.

IV access is obtained through 16G intravenous cannula preloading with balanced salt solution like 0.9% Nacl or lactated Ringer 500 ml is administered.

Procedure

The subarachnoid block consists of 4 p's viz preparation, position, projection and puncture.

Preparation

Preparation of the equipment and drug is essential for performing a subarachnoid block. The choice of drug is based on the duration of block desired, the surgical procedure and patient variables 25G Quinckie - Babcock spinal needle is selected, small size is said to prevent postdural puncture headache (PDPH).

Position

The patient was turned right laterally.

Projection and Puncture

The patient back is painted with betadine and spirit with 2 times each, then dry painting with sterile gauze is done. Then fenestrated draping is done. Identify the midline spines from above downwards.

A line drawn from highest point of iliac crest passes through either spinous process of L_4 or L_4 - L_5 interspace. Traditionally the midline approach with patient in lateral decubitus is most popular. After infiltrating with local anesthetic at L_3 - L_4 interspinous space, the spinal needle is held like a dart and advanced keeping the bevel parallel to the longitudinal dural fibres so that it separate the fibres rather than cut it. The needle is advanced slightly in cephalad direction with the long axis of the vertebral column. A characteristic change in resistance occurs as the needle traverses the supraspinous ligament, interspinous ligament, ligamentum flavum and pierces the arachnoid, which becomes quite recognizable as experience is gained.

The stylet is then removed and appearance of cerebrospinal fluid at the hub of the needle confirms the correct position of the needle tip. The morphine sulphate comes as preservative free as 10 mg / ml in 1 ml ampoule. It is diluted with sterile normal saline to 10 cc so that each ml contains 1 mg/ml. Then ½ cc taken from this, diluted to '1' cc with normal saline taken in sterile cup, so that each ml contains 0.5 mg morphine.

This 1 ml of morphine (0.5 mg) is injected intrathecally without barbotage. After injecting morphine, patient was turned supine.

METHODS OF PAIN MEASUREMENT

Pain is a personal, subjective experience influenced by cultural learning, the meaning of the situation, attention and other psychological variables. Melzack suggested a three dimensional view of pain which comprises of sensory-discriminative, motivational-affective, cognitive-evaluative components.

Methods of Pain Measurement include

1. Verbal rating scale
2. Visual analogue pain scale
3. Mc Gill pain Questionnaire
4. The Descriptive Differential Scale

Visual Analogue Pain Scale

Advantages

1. Simple, efficient, minimally intrusive measure of pain intensity
2. Widely used in clinical as well as research settings

Disadvantages

1. Bias of expectancy for change and reliance on memory
2 It is an assumption that pain is a unidimensional experience

INTRATHECAL OPIOIDS

History

Pert CB and Snyder SH. first identified opiate receptors in the central nervous system in 1973. Subsequently, large populations of these receptors were localized in the dorsal horn of the spinal cord. In 1976, **Yaksh TL** and **Rudy TA** performed animal studies and demonstrated the ability of intrathecal opioids to produce analgesia. In 1979, **Wang** and colleagues reported pain relief using intrathecal morphine in cancer patients and in the same year, **Behar et al** achieved the same result by injecting the drug into the epidural space.

Neuraxial opioids

Placement of opioids in the epidural or subarachnoid space to manage acute or chronic pain is based on the knowledge that Opioid receptors [principally mu receptors] are present in the substantia gelatinosa of the spinal cord [**Cousins** and **Mather**, 1984]. Analgesia produced by neuraxial opioids, in contrast to intravenous [IV] administration of opioids or regional anaesthesia with local anaesthetics, is not associated with sympathetic nervous system denervation, skeletal muscle weakness, or loss of proprioception. Analgesia is dose related.

Spinal opioid receptors - location

Opioid receptors are synthesized in the cell body of the sensory neuron and are transported in both the central and peripheral directions. In the spinal cord, opioid receptors are found in the dorsal horn in the terminal zones of C

fibers primarily in laminae I of the substantia gelatinosa. Spinal opioid receptors are 70% mu, 24% delta and 6% kappa type.

Mechanism of Action

Opioids act as agonists at stereo specific opioid receptors at presynaptic and postsynaptic sites in the central nervous system (principally the brain and spinal cord) and outside the CNS, in peripheral tissues.

The principal effect of Opioid receptor activation is a decrease in neurotransmission by presynaptic inhibition of neurotransmitter (acetylcholine, dopamine, norepinephrine, substance P) release, although postsynaptic inhibition of evoked activity also occurs. The biochemical events following opioid receptor activation are characterized by increased potassium conductance (leading to hyperepolarisation), calcium channel activation, or both, which produced an immediate decrease in neurotransmitter release.

Activation of opioid receptors in the primary afferent neurons may either directly decrease neurotransmission or inhibit the release of excitatory neurotransmitters such as substance P.

Opioid Receptors

	Mu_1,	**Mu_2**	**Kappa**	**Delta**
Effect	Analgesia (supra spinal and spinal) Euphoria Low abuse potential Miosis Bradycardia Hypothermia Urinary Retension	Analgesia (Spinal) Depression of Ventilation Physical dependence Constipation (marked)	Analgesia (Supraspinal and spinal) Dysphoria Sedation Low abuse potential Miosis Diuresis	Analgesia (supraspinal and spinal) Depression of ventilation Physical dependence Constipation (minimal) Urinary retention
Agonists	Endorphins Morphine Synthetic Opioids	Endorphins Morphine Synthetic opioids	Dynorphine	Enkephalins
Antagonists	Naloxone Naltrexone Nalmefene	Naloxone Naltrexone Nalmefene	Naloxone Naltrexone Nalmefene	Naloxone Naltrexone Nalmefene

Neuraxial Opioids

Based on the knowledge, Opioid receptors (principally mu receptors) are present in the substantia gelatinosa of the spinal cord.

In contrast to intravenous administration of opioids (or) regional anaesthesia with local anaesthetics, analgesia produced by neuraxial opioids is not associated with sympathetic nervous system denervation, skeletal muscle weakness or loss of proprioception. Analgesia is dose related and is specific for

visceral rather than somatic pain and neuraxial opioid decreases the minimum alveolar concentration (MAC) of the volatile anaesthetics.

Spinal Opioid Receptors - Location

Opioid receptors were synthesized in the cell body of the sensory neuron and were transported in both the central and peripheral directions. In the spinal cord, Opioid receptors are found in the dorsal horn in the terminal zones of C fibers primarily in lamina I of the substantia gelatinosa. Spinal opioid receptors are 70% mu, 24% delta and 6% kappa.

Mechanism of Action

Spinal opioids act at nerve synapses either presynaptically [as neuromodulators] or postsynaptically [as a neurotransmitter]. Stimulation of presynaptic receptors is associated with hyperpolarization of the terminal and reduced substance P release. This relates primarily to inhibition of voltage gated calcium channels. Postsynaptic membranes contain opioid receptors linked to potassium channels. Stimulation of these receptors enhances outward flow of potassium thereby stabilizing the membrane, making it less sensitive to neurotransmitters. Second messengers [G proteins] carry out these actions.

With the injection of an opioid into the CSF, a reservoir of drug is created that passively diffuses into the dorsal horn of the spinal cord where it exerts its action by binding to opioid receptors.

Pharmacokinetics

The onset of analgesic effect following intrathecal administration of an opioid is directly proportional to the lipid solubility of the drug, whereas the duration of effect is longer with more hydrophilic compounds. Opioids placed in the epidural space undergo significant systemic absorption and passage into the subarachnoid space. Vascular absorption after intrathecal administration of opioids is insignificant. Cephalad movement of opioids in the CSF is dependent on lipid solubility. Lipid soluble opioids like fentanyl are limited in the cephalad migration by uptake into the spinal cord, while hydrophilic opioids like morphine remain in the CSF for transfer to more cephalad locations.

Loss of analgesia after intraspinal injection primarily results from clearance of drug from the site of action. Intrathecal opioids were eliminated by diffusion along the neuraxis and vascular absorption. It is not yet established what role metabolism plays in the termination of action of intrathecal opioids.

Tolerance

Decrease in effect over time to a given dose of drugs has been demonstrated with intrathecal opioids. There is good evidence in support of the glutamate receptor of the NMDA type to be involved in the mechanism of tolerance.

Benefits

- Long lasting post operative analgesia after a single injection
- Precise and reliable placement of low concentration of drug near its site of action.

The principle disadvantage was lack of titrability and need to either repeat the injection or consider other options when the analgesic effect of the initial dose wanes. Nevertheless, common clinical experience is greatly diminished. Can be satisfactorily managed by other modalities.

Side Effects

1. Pruritus

Pruritus is the most common side effect and is more likely to be localized to the face, neck or upper thorax, often elicited only after direct questioning, particularly in obstetric patients, due to the interaction of estrogen with opioid receptors. It is due to cephalad migration of the opioid in CSF and subsequent interaction with opioid receptors in the trigeminal nucleus. Naloxone, an opioid antagonist is effective in relieving pruritus.

2. Urinary Retention

It is common in young males and with spinal and epidural administration than after IM or IV administration.

It is most likely due to interaction with opioid receptors located in sacral segment of the spinal cord and inhibition of sacral parasympathetic nervous

system outflow, which causes detrusor muscle relaxation and increase in bladder capacity, leading to urinary retention and was readily reversed with Naloxone.

3. Depression of ventilation

This is the most serious side effect of neuraxial opioids which may occur within one minute or may be delayed for hours, requiring intervention.

Early depression of ventilation occurs within 2 hours of neuraxial injection of opioid and results from systemic absorption of the lipid soluble opioids. Eg. Fentanyl, Sufentanil.

Delayed depression of ventilation occurs more than 2 hours and reflects cephalad migration of the opioid in the CSF and subsequent interaction with the opioid receptors in the ventral medulla. Eg. Morphine.

Factors that increase the risk of depression of ventilation.

High opioid dose
Low lipid solubility of opioids
Concomitant administration of parenteral opioids
Lack of opioid tolerance
Advanced age

4. Sedation - Dose related particularly with morphine.

5. CNS excitation

Tonic skeletal muscle rigidity resembling seizure activity occur following large IV doses of opioids but rarely with neuraxial administration. Cephalad migration in the CSF and interaction with non-Opioid receptors in the brain stem (or) basal ganglia is the most likely explanation, inhibition of the inhibitory neurotransmitters.

6. Viral reactivation

Reactivation of herpes simplex labialis may occur 2-5 days after epidural administration.

7. Neurotoxicity

Animal and human studies have not demonstrated neurotoxicity with any of the commercially available preservative free opioid agents administered by the subarachnoid route.

Advantages of Intrathecal Morphine

1. Ease of administration
2. Single shot technique
3. No need of costly equipment to administer it
4. Definitive end point of success, like aspiration of CSF

Disadvantages

1. It causes delayed respiratory depression
2. Need for monitoring at PACU / High dependency Unit
3. Lack of titrability
4. Postdural Puncture headache (PDPH)

Morphine Sulfate

It is belongs to phenanthrene alkaloids. It is a prototype of drug to which all the Opioid analgesics potency are compared.

Chemically it has a rigid five ring structure conforms to a "T" shape, with a phenyl piperidine ring forming a cross bar and a hydroxylated aromatic ring in the vertical axis.

Morphine has major effects in the CNS and the gastrointestinal systems, but other systems are also affected.

Analgesia

Morphine act selectively at μ_1, μ_2 opioid receptors on neurons that transmit and modulate nociception, leaving other sensory modalities and motor functions intact.

At the spinal cord level, morphine acts presynaptically on primary afferent receptors to decrease the release of substance p and hyperpolarizes postsynaptic neurons in substantia gelatinosa of dorsal spinal card to decrease

afferent transmission of nociceptive impulses. Spinal morphine analgesia is mediated by μ_2 opioid receptors.

Supraspinal opioid analgesia originates in the periaqueductal grey matter (PAG), the locus ceruleus (LC), and nucleus within medulla, the nucleus raphe magnus (NRM).

Other Side Effects

1. Cognitive and five motor impairment showing of E.E.G. activity. Morphine inhibits me release of several pituitary hormones both directly and indirectly.

2. Respiratory depression: It products respiratory depression and shift right ward and decrease the slope of ventilatory response to CO_2 curve.

3. Cough

   It suppresses cough reflex by acting at medullary cough centre.

4. Nausea and vomiting

   It is most frequency side effect of morphine due to stimulation of chemoreceptor trigger zone (CTZ) in medulla, pharynx, GI tract and have rich opioid receptors.

   It delays gastric emptying.

5. Urinary retention: Seen after systematic and spinal morphine administration but is reversible with naloxone.

Histamine release

Occurs in a dose dependant manner.

Cardiovascular effects

It can produce arteriolar and venous dilatation decreased peripheral resistance and inhibition of baroreceptor reflexes. It has central sympatholytic action and leads to hypotension in who have high sympathetic tone.

It can cause bradycardia due to both sympatholytic and parasympathothimetic actions. I.v 0.01 to 0.2 mg/ kg Dosage is used for Premedication for balanced anesthesia.

Pharmacokinetics

pH 7.9; percentage non ionized at pH 7.4 ; protein binding 35%.It is hydrophilic in nature 35% protein bound and mostly to albumin. Morphine may be administered orally, subcutaneously, intrathecally and intravenously. Hepatic clearance is high. It has clearance of 1050 ml/min

Poor penetration in CSF is due to

a. Poor lipid solubility
b. High degree of ionization at physiological pH
c. Protein binding
d. Rapid conjugation with glucuronic acid.

Metabolism

The principal pathway of metabolism is conjugation with glucuronic acid in hepatic and extra hepatic sites especially kidneys. Its metabolites one morphine 6-glucoronide and morphine - 3 - Glucuronide when former is active and later is an inactive metabolite.

Duration of action of Morphine peak analgesic effects in 20 to 60 minutes that last for 12 hrs when dosing range from 0.25 mg to 1 mg given intrathecally but doses in the range of 0.25 m to 0.5 mg generally maintain analgesic efficacy while minimizes ventilatory depression.

REVIEW OF LITERATURE

Identification of opiate receptors in the brain and spinal cord and the role of morphinomimetic substances in the mechanisms of pain perception have led to the use of intrathecal opioid in animals and man for the relief of pain.

Intrathecal Opioid receptors and Analgesia

Pert CB and Sinder SH [1973] demonstrated the presence of opioid receptors ion high density in the dorsal horn of the spinal cord.

Yaksh TL and Rudy TA[53] [1976] published a study on the effectiveness of intrathecal morphine for relief of experimental pain in rats. This report initiated a series of trails in main.

Behar M et al[1] [1979] reported the first effective use of epidural opioids in human while **Wang JK et al**[2] [1979] reported the first controlled study of intrathecal opioids in human. They demonstrated that small doses of morphine given intrathecally or extradurally produced long lasting relief of chronic and post operative pain in man. The use of these methods spread rapidly and became clinically accepted long before data from controlled studies were published.

Crawford JS[45] [1980] claimed that spinal opioids act predominantly on the brain.

Willer JC and **Bussel B**[52] [1980] and **Maruyama Y et al** [1980] suggested a selective spinal analgesic effect in humans.

Willer JC and Bussel B[52] [1980] and **Yaksh TL** [1981] suggested that opioids act on presynaptic and postsynaptic receptors in th4e substantia gelatinosa of spinal cord dorsal where they inhibit neurone cell excitation.

Nicol et al [1991] studied densities of various drugs used intrathecally. They used 5% glucose as a vehicle for use as a hyperbaric solution along with opioids. They concluded that all drugs dissolved in 5% glucose were hyperbaric in comparison with CSF at room and body temperature.

ANALGESIC EFFECT OF INTRATHECAL MORPHINE

JA Eandi, RW De vere White retrospectively analysed the analgesic efficacy and surgical out come of single dose intrathecal long acting morphine (0.25 – 0.5mg) and postoperative ketrolac who underwent radical retropubic prostatectomy (RRP). They conducted single preoperative injection of intrathecal morphine sulphate combined with rescue I.V. Ketrolac. They concluded that IT Morphine results in effective analgesia in the post-operative period , diminished supplemental narcotic requirement and high patient satisfaction.

Jean-Michel Devys,Anne Mora, Benoit Plaud et al (2003) studied the analgesic effect and sideeffects produced by IT Morphine 0.4 mg in 60 adult patients undergoing major abdominal surgery. The control group received PCA-Morphine. VAS scores, supplemental analgesia consumption, patient satisfaction, arterial saturation, respiratory rate, nausea, vomiting and Pruritis were studied. VAS scores were lower in the IT morphine group for the first 48 hours, both at rest and during coughing. No patient had a respiratory rate < 10

in both the groups but IT morphine group needed supplemental oxygen to maintain SaO2. Nausea and Vomiting was more in the IT morphine group.

ASK Kwan, BB.Lee, T.Brake et al (1997) studied the effect of addition of 0.2 mg of preservative free morphine 0.2 mg to 2.2 ml of hyperbaric bupivacaine (2.6 ml)SsS in patients undergoing hip surgeries. Post-operative VAPS score was used to assess pain every 2 hours for the first 24 hour period. Time to first rescue analgesia demand was noted. The duration of analgesia was defined as time from performance of SAB to the time when patient made first request for analgesia. Respiratory rate, sedation scores, Nausea, vomiting, Hemodynamics and other complications were monitored. The morphine group had significantly lower VAPS score when compared to control group. There was no incidence of hypopnoea or hemodynamic instability. Sedation scores were within acceptable range. They concluded that IT morphine provides excellent post-operative analgesia for the first 48 hours with low propensity to side effects. The reported optimal analgesia dose appears to lie between 0.3 mg and 1.0 mg, while significant respiratory depression occurs with doses of 0.8 to 1.0 mg.

Gwirtz KH,[10] **Young JV**, **Byers RS**, **Alley C**, **Levin K**, **Walker SG**, **Stoelting RK** published a retrospective study on the safety and efficacy of intrathecal opioid analgesia for acute postoperative pain over a period seven years for 5969 surgical patients at Indiana University Hospital undergoing major urologic, orthopedic, general/ vascular, thoracic, and non-obstetrical gynecologic surgery. A scale of 1-10 was used to quantify each patient's satisfaction with analgesia. The incidence of side effects, complications, and

naloxone usage was also recorded and tabulated. They concluded intrathecal opioid analgesia was used to control acute postoperative pain on nearly 6000 patients, resulting in a high degree of patient satisfaction and a low incidence of side effects and complications. Side effects were minor and easily managed. Pruritus was the most common (37%). Respiratory depression was the least common (3%), easily detected by nursing observation, never life threatening, and always responsive to treatment with naloxone. There were no deaths, nerve injuries, central nervous system infections, or naloxone-related complications.

Kirson.L.E,**GoldmanJM**, **et al**[8] studied 30 patients undergoing lidocaine spinal anesthesia for transurethral resection of the prostate (TURP) were studied to evaluate the effectiveness of low-dose intrathecal morphine (ITM) for postoperative analgesia. In a double-blinded fashion, groups of ten patients received either 0.1 mg morphine, 0.2 mg morphine, or placebo (control group) intrathecally with lidocaine 75 mg. Standard postoperative analgesics were available to all patients. Patients receiving 0.1 mg or 0.2 mg morphine reported significantly less postoperative pain as assessed by an inverse numerical visual pain scale and required significantly fewer postoperative analgesic interventions than the control group. There was no difference between the 0.1 mg ITM and 0.2 mg ITM groups with regard to severity of postoperative pain or analgesic requirements. The incidence of nausea and vomiting was significantly higher in the group receiving 0.2 mg ITM than in the control group. Six patients (60%) in the 0.2 mg ITM group, two patients (20%) in the 0.1 mg ITM group, and one patient (10%) in the control group experienced nausea and vomiting. No clinically evident respiratory depression occurred in any of the subjects. The authors conclude that administration of 0.1

mg or 0.2 mg of morphine intrathecally is effective in reducing postoperative pain following TURP and that 0.1 mg ITM is not associated with nausea and vomiting.

T.K. Abboud, A Pror[6]; from the university of southern California studied the effect of mini dose intrathecal morphine for relief of post caesarean pain. Group I received 0.25mg IT morphine. Group – II received 0.1mg IT morphine combined with Bupivacaine. Group III received 8mg subcutaneous morphine. They concluded that in Group I & II patients post op analgesia was 27.7$\pm$ 4.0 hrs and 18.6 $\pm$ 0.9hrs respectively. Group III needed an analgesic within 3 hrs of spinal anaesthesia and respiratory depression was more in Group III.

John R. Gray, Glenn A. Fromme showed that post operatively analgesic duration following post thoractomy after intra morphine in the lumbar area 10ug/kg morphine either in dextrose hyperbaric or with normal saline (Isobaric) showed that duration of analgesic was longer with morphine in normal saline group than in hyperbaric group ($P<0.04$).

Ganesh A, K.M.A. Cucchiaro studied the effect of low dose (4-5μg/kg) intrathecal morphine for post operative pain management after various surgical procedures in children. They had shown that median maximum pain score using FLACC score and numeric verbal rating scale was '0'. Mean time for first rescue opioid was 22.4$\pm$16.9 hours. Nausea or vomiting, Pruritis and urinary retention was 32%, 37% and 6% respectively.

Nordberg G. Heduer T, Dalhlstrom B (1984) studied the pharmacokinetic aspects of intrathecal morphine analgesia in 15 patients undergoing thoractomy. The study indicates the significant pharmacokinetic parameter related to the long duration of analgesia after intrathecal morphine administration probably is the high CSF concentration found since the rate of elimination from CSF is similar to what is reported for morphine in plasma.

Andrew et al (2000) studied the efficacy and safety of low dose ITM (Intrathecal Morphine) for postoperative analgesia in children and demonstration that ITM in pediatric population can provide safe and dependable period of analgesia. The average time for any patient requiring opioid administration (Parental or oral) was approximately 8 hours.

Kirson LE, Goldman JM, Scover RB did a double blind study in 30 patients undergoing TURP. In a double blinded fashion groups of 10 patients received either 0.1mg morphine, 0.2mg (ITM) morphine placebo patients receiving 0.1mg or 0.2mg (ITM)morphine reported significantly less post operative pain as assessed by an universal numerical visual pain scale and required significantly fewer postoperative analgesia.

Kwan As, Lee BB, Brake T studied the efficacy of ITM for postoperative analgesia in Chinese patients undergoing surgery to repair fractured hips. The results show the median pain free period in prolonged (i.e. 16-24 hrs) in morphine group compared with control group (2-24 hrs).

Gwirtz et al[10] studied the efficacy and safety of intrathecal morphine analgesia for acute postoperative pain, and showed that there is a higher degree of patient satisfaction and low incidence of side effects and complications.

Complications of intrathecal opioids

Glynn CG et al[48] [1979] and **Davies GK et al**[46] [1980] reported respiratory depression following spinal morphine.

Glynn CG al [1979] reported a respiratory depression with rostral spread of spinal opioids. He noted a delay of upto 11 hours before onset of respiratory depression following spinal morphine.

Jones RDM[20] [1980] reported that naloxone was effective for reversing such respiratory depression without reversing analgesia.

Reiz and Westberg [1980] and **Yaksh TL**[53] [1981] and **Samii J, Chanin M and Viars P** [1981] reported adverse reactions such as Pruritis and urinary retention after intrathecal administration of opioids.

Oyama T [1980] observed that Pruritis did not occur following intrathecal endorphin.

Bromage PR et al[42] [1982] suggested that pruritus may be due to alterations in sensory modulations following opioid spread over the spinal cord to the brain. They also found naloxone to be effective in the control of pruritus in some cases.

Roscow CE et al [1982] reported pruritus associated with spinal opiodis but was a opinion that it was unlikely to be due to histamine release since pruritus occurred with fentanyl which does not cause systemic release of histamine.

Lam et al [1983] reported that delayed respiratory depression does not occur after epidural fentanyl which has lipophilic properties similar to pethidine.

Cousins MJ and Mather LE al [1984] suggested that the pruitus was unlikely to be due to the preservatives in the opioid since it occurs also with preservative free preparations.

MATERIALS AND METHODS

This study was conducted at Government General hospital, Madras Medical College General between July 2008 to A September 2008 at General surgical operation theatre.

1. The study was done after getting Institutional Ethical committee approval

2. Written informed consent were obtained from all patients included in the study.

All patients were explained preoperatively about the procedure and visual analog scale (Pain score) 10 cm scale so that it can be effectively used by the patient during the postoperative period.

Inclusion Criteria	Exclusion Criteria
1. A.SA I, II, III patients	1. Patient refusal
2. Those patients who are undergoing upper and bower abdominal Surgeries	2. Contraindication to subarachnoid block
	3. Hypersensitivity to study group
	4. Difficult airway MMS** >3
	5. Hepatic and renal dysfunction
	6. Not meeting inclusion criteria

MMS- Modified mallampatti score.

50 patients of ASA physical status I, II and III undergoing both upper and lower abdominal surgeries like partial Gastrectomy, open cholecystectomy, incisional hernia, hemicolectomy and laparotomy under general anesthesia.

The patients are categorized into one of two groups.

Group M - Morphine - Study Group

Group C - Control Group

All patients were assessed preoperatively using standard protocols and underwent preoperative evaluation.

All patients received Premedication T.alprazolam using T.Ranitidine 150 mg P.O. the night before surgery and on the day of surgery 2 hours before operation P.O. with sips of water.

Preservative free Morphine sulphate comes in two strengths 15 mg / ml and 10 ml / ml ampoule manufactured by verve health care Ltd. We used 10 mg/ml of morphine sulphate (Vermor - 10). This was taken in sterile 10 ml syringe mixed with sterile Normal saline by the incharge Anaesthesiologist uninvolved in the administration of Subarachnoid block or in further conduct of the study . This solution was isobaric to cerebrospinal fluid .

In the OT, patients were hooked on to monitors like E.C.G., pulse oximetry and Non invasive BP. After Baseline evaluation and recording of baseline data, Two 16G large IV cannula was started in both forearms. 500 ml of balanced salt solution was administered as preload. The patient was turned to right lateral position. Back was painted with antiseptic solution and draped.

Morphine is taken in 0.5 mg diluted to 1 cc with Normal saline. Subarachnoid block was performed with 25G Quinckie Babcock spinal needle at the L3-L4 ISS and after confirming free flow of CSF , the study drug ie:1 ml of preservative free morphine 0.5 mg, was administered with due precautions. Then patient was assumed post-spinal supine position. The patient was observed for 10 minutes before induction of general anaesthesia to look for any immediate untoward events.

After preoxygenation with 100% oxygen (O_2) for 5 minutes.

GA was administered composed of inj. Glycopyrrolate 10µg /kg + Fentanyl 2µg/kg i.v., and Induction with inj. Thiopentone sodium 5 mg / kg i.v, then muscle relaxant i.v Vecuronium 0.12 mg/kg was given and mask ventilation done with oxygen 50% with Nitrous oxide 50% with volatile agent isoflurane1%. If airway difficulty is expected (MMS ≥ 3), then suxamethonium was used for intubation.

Laryngoscopy was done and intubated with 8 or 8.5 mm cuffed Endotracheal tube orally for male patients and 7 or 7.5 mm orally in female patients. Bilateral air entry was checked, tube was fixed, and cuff inflated.

All patients were catheterized by operating surgeon to monitor urine output. Then vitals were recorded every 5 minutes until the end of surgery PR, BP, SPo2. IV fluids were given according to Body weight, blood loss and 3rd space loss.

Injection Diclofenac sodium 75 mg IV infusion was started after one hour of surgery for both groups. Fentanyl supplements of 20µg were used as and when necessary.

At the end of surgery after replacing blood losses and fluids and after recovery from muscle relaxants by clinical assessment, patient was reversed with inj. Neostigmine 0.05 mg/kg + Glycopyrolate 10µg/Kg i.v. After thorough suctioning and good respiratory attempts patient was extubated on table if hemodynamically stable.

Then patient was shifted to post anaesthetic care unit (PACU) with oxygen supplementation. PACU PG & PACU consultant were in charge of monitoring pain scores and further analgesic intervention as per PACU protocols.

In PACU patient all vital parameters were recorded, oxygen by Hudson mask 4 litre / minutes was given, and 30° Head up was given.

The degree of pain was assessed by visual analog scale (VAS). In PACU V.A.S. was done every hour until '4' hour and thereafter every '2' hours for 24 hours.

VAS was also noted whenever patient complained of pain and injection diclofenac sodium 75 mg was given intramuscularly as intial analgesic in Morphine group. Still if VAS>4 Rescue analgesic was used in the form of titrated boluses of Fentanyl 20µg/kg and it was titrated to patients response.

In control group, inj. diclofenac 75 mg Im b.d. and inj.Tramadol 100 mg i.v. t.d.s was given routinely as per PACU Protocol. If VAS of control > 4 then Rescue analgesic inj. Fentanyl 20 µg boluses were given, titrated to patient responses.

Recovery characteristics include VAS score; Ramsay sedation scale, Postoperative HR, BP. Saturation, complications and adverse effects of opioids were monitored and noted.

The other parameters monitored in the post-operative period included

Time for Ist demand analgesia,
No. of Analgesia doses in Ist 24 hours
No. of NSAID doses in Ist 24 hours
No. of Rescue analgesic does in 24 hour .

The complications monitored included

1. Retention of urine is common after spinal opioids but all our cases patients were catheterized and hence it was not evaluated.

2. Respiratory depression. It is defined as a respiratory rate < 8 / min and or oxygen saturation < 90%. This was planned to be managed with bag and make ventilation or intubation and I.P.P.V. if necessary naloxone 0.1 mg intravenously administered every 5-10 minutes till normal breathing pattern was established.

3. Nausea and vomiting

   Patients were observed for nausea and vomiting vomiting was managed with inj. ondansetron 8 mg intravenously.

4. Pruritis: If distressing , it was planned to be treated with Inj. Promethazine 25 mg Intravenously.

5. Hypotension was defined as systolic blood pressure < 90 mm of Hg of fall in systolic pressure > 30% from baseline. This was planned to be managed with intravenous Ephedrine in increments of 6 mg.

6. Bradycardia : It was defined as heart rate less than 60 beats per minutes and this was planned to be managed with inj. Atropine 0.01 mg/kg intravenously

7. Sedation

   The level of sedation was scored according to the six grade score devised by Ramsay and colleagues.

   1. Anxious and agitated or restless or both.
   2. Cooperative oriented and tranquil
   3. Responds to commands only
   4. Asleep with brisk response to light glabellar tap or loud auditory stimulus.
   5. Asleep with sluggish response to stimulus.
   6. Asleep with no response to stimulus.

A sedation score greater than '4' was considered significant. Patient was observed for 24 hours then if hemodynamically stable then patients was shifted to postoperative ward for continued care. Patient study was completed after 24 hours of intrathecal morphine.

Study

A total of 50 cases each were randomly allocated to one of the following, two groups viz Group – M(Morphine) and Group - C (Control).The information collected regarding all the selected cases were recorded in a Master Chart. Data analysis was done with the help of computer using **Epidemiological Information Package (EPI 2002).**

Using this software, frequencies, percentages, means, standard deviations, chi square and 'p' values were calculated. Kruskul Wallis chi-square test was used to test the significance of difference between quantitative variables and Yate's test for qualitative variables. A 'p' value less than 0.05 is taken to denote significant relationship.

OBSERVATION & RESULTS

The study was conducted at Government General Hospital, Chennai. Fifty patients were included in this double blind randomized control study.

The patients were divided into two groups of twenty-five each, patients in Group-M received intrathecal Morphine 0.5 mg in '1' ml at L_3 - L_4 interspace and routine General anesthesia and Group - C received only balanced General anaesthesia followed by multimodal analgesia protocol followed at the institute which consisted of a combination of analgesic Inj.Tramadol hydrochloride plus Inj. Diclofenac Sodium. Rescue Analgesic in the form of titrated boluses of Fentanyl Citrate was used as and when required to meet titrated end points based on VAS scores.

Demographic Data :

Table 1 : Age

Age Group	Morphine Group		Control Group	
	No	%	No	%
Up to 20 Yrs	1	4	1	4
21-30	5	20	7	28
31-40	6	24	6	24
41-50	7	28	5	20
51-60	3	12	5	20
Above 60 years	3	12	1	4
Total	25	100	25	100
Mean	41.0 Years		39.2 Years	
SD	13.8 Years		12.6 Years	
'p'	0.6835 Not Significant			

Both the groups were comparable with respect to age, height, weight, baseline pulse rate, systolic and diastolic blood pressure, respiratory rate and oxygen saturation. The duration of surgery was also comparable between the two groups. This was not statistically significant between the groups in demographic aspect.

Table 2 : Sex

Sex	Morphine Group		Control Group	
	No	**%**	**No**	**%**
Male	14	56	15	60
Female	11	44	10	40
Total	25	100	25	100
'p'	0.7767 Not Significant			

There were 14 males, 11 females in Morphine group and in control group were 15 males and 10 females, and it was not significant which has P value 0.7767. The time for Ist demand analgesia in the postoperative period in Group-M is 13.8hours and in Group–C 1.0 hour and statistically significant.(p=0.00079)

Table 3: Analgesic requirements

Drug use	Morphine Group		Control Group		'p'
	No.	**%**	**No.**	**%**	
Time for Ist PT analgesic demand (in hours)	13.8	11.9	1.0	1.0	**0.0079 Significant**
Number of analgesic demand in 24 hours	1.56	2.31	4.2	2.93	**0.0002 Significant**
Total NSAID used in 24 hours	0.44	0.51	-	-	-
Inj. Fentanyl used in 24 hours((µg)	1.1	1.94	86	72.6	**0.0003 Significant**

The number of demand analgesic in 24 hours is 1.56 in group-M vs 4.2 in group-C and it is statistically significant (p=0.0002)

The total rescue analgesic inj. Fentanyl used in group-m is 1.1 vs. 86 in group-c and it is statistically significant. (p=0.0003).

Table 4 : Intra Operative systolic B.P.

Intra Operative Systolic B.P at minutes	Morphine. Group		Control Group		p	Significance
	Mean	S.D	Mean	S.D		
Baseline	124	17.9	125.1	17.7	0.7729	Not Significant
15	123	16.4	122.4	14.8	0.7993	Not Significant
30	119	17.1	121.5	15.5	0.4504	Not Significant
45	123	16.1	119.2	15.1	0.4467	Not Significant
60	120	14.7	122.9	12.8	0.4115	Not Significant
75	120	14.0	121.4	14.4	0.9753	Not Significant
90	116	15.5	122.3	13	0.1206	Not Significant
105	117	9.7	121.9	13.7	0.3503	Not Significant
120	117	16.1	119.1	14.3	0.6378	Not Significant
135	118	12.5	121.0	14.4	0.4647	Not Significant
150	120	11.9	119.4	13.4	0.7943	Not Significant
165	117	12	118	14.1	0.7559	Not Significant
180	117	16	117.6	13.4	0.8157	Not Significant

The mean intraoperative systolic BP was 124 in Morphine group and 125 in control group and statistically not significant.

Table 5 : Intra Operative Diastolic B.P.

Intra Operative D.B.P. at minutes	Morphine group		Control group		p	Significance
	Mean	S.D	Mean	S.D		
Baseline	80.1	7.9	82.8	10.8	0.3901	Not Significant
15	80.2	10.0	81.3	12.1	0.7699	Not Significant
30	78.0	11.3	80.3	10.4	0.3404	Not Significant
45	77.8	9.9	79.5	12.6	0.4892	Not Significant
60	77.2	8.6	82.5	11.7	0.1019	Not Significant
75	76.8	9	82.0	9.7	0.1046	Not Significant
90	75.3	9.3	81.4	8.3	**0.0114**	**Significant**
105	76.4	8.1	79.3	9.3	0.3937	Not Significant
120	76.5	11.2	78.7	8.4	0.7631	Not Significant
135	79.2	7.5	80.4	9.4	0.5076	Not Significant
150	78	7.9	81.2	9.4	0.1445	Not Significant
165	76.7	7.4	78.6	9.6	0.3202	Not Significant
180	77.2	8.4	78.8	9.0	0.4659	Not Significant

Intra operative diastolic Blood pressure was compared between both groups had 80 and control group 82 and P value as 0.39 and not significant.

Table 6 : Intra Operative Mean Arterial B.P.

Intra Operative MAP at minutes	Morphine group		Control group		p	Significance
	Mean	S.D.	Mean	S.D.		
Baseline	94.6	10.2	96.9	12.6	0.5527	Not Significant
15	95.0	11.7	95	12.6	0.9923	Not Significant
30	92.3	12.9	94	11.3	0.3366	Not Significant
45	92.9	11.1	92.8	12.9	0.8842	Not Significant
60	92.4	9.7	96	11.1	0.1564	Not Significant
75	91.3	9.4	95.1	9.9	0.1679	Not Significant
90	89	10.3	95	9.1	**0.0262**	**Significant**
105	90	7.9	93.5	9.6	0.3035	Not Significant
120	90.1	12.2	92.2	9.4	0.5473	Not Significant
135	92.4	8.1	93.9	10.7	0.5409	Not Significant
150	92.2	8.2	93.9	10.2	0.4093	Not Significant
165	90.4	7.9	91.8	10.5	0.4847	Not Significant
180	90.5	9.8	91.8	9.8	0.8008	Not Significant

The mean arterial pressure is not significant between both groups and group-M had 94 ± 10.8 and in group-C 96 ± 12.6 and P value 0.5527. But is significant at 90^{th} minute (P = 0.0262). Probably it is associated with onset of action of IT morphine.

Table 7 : Intra Operative pulse Rate

Intra Operative PR at minutes	Intra Operative Pulse Rate				p	Significance
	Morphine group		Control group			
	Mean	S.D	Mean	S.D		
0	90	14.8	91.2	16.9	0.7924	Not Significant
15	91.5	17.0	91.3	19.1	0.5998	Not Significant
30	90.8	16.5	88.9	14.3	0.734	Not Significant
45	88	16.7	89.1	16.7	0.7634	Not Significant
60	88.2	17.3	87.4	19.3	0.7633	Not Significant
75	85.8	16.7	85.8	19.5	0.9227	Not Significant
90	85.1	18.2	83.3	17.2	0.969	Not Significant
105	83.5	20.3	81.1	17.3	0.8536	Not Significant
120	84	21.5	79.4	16.0	0.4374	Not Significant
135	86.8	21.7	78.3	16.4	0.1508	Not Significant
150	86.3	22.1	79.6	16.2	0.2989	Not Significant
165	86.6	22	80.1	16.2	0.3983	Not Significant
180	83.5	19.2	82.8	16.9	0.9768	Not Significant

Intra operative pulse rate in group –M was 90 ± 14 Vs 91 ± 16.9 in group-C and it is statistically not significant.

Table 8: Post Operative VAS

Post Op. Vas at hours	M Group		Control Group		'p'	Significance
	Mean	SD	Mean	SD		
0 hours	4.64	1.41	5.0	1.41	0.3448	Not Significant
2 hours	4.64	1.41	5.24	0.88	0.0751	Not Significant
4 hours	3.76	0.88	4.6	0.76	**0.0009**	**Significant**
8 hours	3.8	0.76	4.4	0.76	**0.0055**	**Significant**
10 hours	3.8	0.71	3.92	0.49	0.2868	Not Significant
12 hours	3.6	0.58	4.04	0.61	**0.0137**	**Significant**
14 hours	3.72	0.54	3.76	0.66	0.9177	Not Significant
16 hours	3.84	0.47	3.96	0.45	0.3609	Not Significant
18 hours	3.84	0.47	3.88	0.53	0.8	Not Significant
20 hours	3.84	0.47	4.08	0.76	0.199	Not Significant
22 hours	3.88	0.44	4.4	0.65	0.0017	**Significant**
24 hours	3.92	0.49	3.84	0.55	0.5704	Not Significant

Post operative visual analog score in Group-M was 4.64 vs 5 in group-C. But it was highly significant at 2, 4, 8, 12, 20 Hours and. However, it was not significant at postoperative zero hour, 14, 16, 24 hours. Intrathecal Morphine seems to have a certain lag in onset of analgesia.

Table 9 : Post Operative RSS

Post Op. RSS at hours	Morphine Group		Control Group		'p'	Significance
	Mean	SD	Mean	SD		
0	2.16	0.8	1.6	0.76	**0.0156**	**Significant**
2	2.32	0.47	1.56	0.65	**0.0001**	**Significant**
4	2.28	0.46	1.56	0.58	**0.0001**	**Significant**
6	2.32	0.48	1.68	0.56	**0.0002**	**Significant**
8	2.28	0.46	1.68	0.56	**0.0003**	**Significant**
10	2.24	0.52	1.88	0.44	**0.0124**	**Significant**
12	2.24	0.44	1.92	0.4	**0.0113**	**Significant**
14	2.24	0.44	2.0	0.29	**0.0281**	**Significant**
16	2.24	0.44	2.04	0.2	**0.0437**	**Significant**
18	2.32	0.48	2.04	0.2	**0.0107**	**Significant**
20	2.36	0.49	2.04	0.2	**0.0051**	**Significant**
22	2.32	0.48	2.04	0.2	**0.0107**	**Significant**
24	2.28	0.46	2.04	0.2	**0.0219**	**Significant**

Postoperative Ramsay sedation scale is 2.16 in Group-M, 1.6 in Group-C, This is statistically significant (P - 0.0156).

Table 10 : Post Operative Heart Rate

Post Op. Heart rate at hours	Morphine Group		Control Group		'p'	Significance
	Mean	SD	Mean	SD		
0	85	12.7	101	13.9	**0.0002**	**Significant**
2	80	10.2	100	11.4	**0.0001**	**Significant**
4	76	9.8	99	12.2	**0.0001**	**Significant**
8	76	11.3	99	10	**0.0001**	**Significant**
12	79	11.5	99	11.3	**0.0001**	**Significant**
16	78	9.1	100	10.1	**0.0001**	**Significant**
20	78	8.2	100	9.6	**0.0001**	**Significant**
24	77	8.5	102	8.8	**0.0001**	**Significant**

The postoperative heart rate was in group-M Vs group -C are 85±12.7 and 101 ± 13.9 respectively and it is statistically significant (P=0.0002) during the postoperative period. The Postoperative changes in heart rate are significant at 2, 4, 8 and 24 hours after intrathecal Morphine injection.

Table 11: Post Operative Systolic B.P

Post Op. SBP at hours	Morphine Group		Control Group		'p'	Significance
	Mean	SD	Mean	SD		
0	116	23.4	138.7	22.2	**0.0018**	**Significant**
2	113.0	21.6	135.2	22.2	**0.0033**	**Significant**
4	111.3	22.2	140.3	17.5	**0.0001**	**Significant**
8	109	22.4	142.4	16.3	**0.0001**	**Significant**
12	110.4	20.5	141.5	18.1	**0.0001**	**Significant**
16	109.2	19.8	138.4	18.4	**0.0001**	**Significant**
20	107.5	18.4	139.8	18.7	**0.0001**	**Significant**
24	107.2	17.0	137.8	17.2	**0.0001**	**Significant**

Post operative systolic BP was 116 ± 23.4 in Group - M Vs 138 ± 22 in control group which is statistically significant p = 0.0018.

Table 12 : Post Operative Diastolic B.P.

Post Op. DBP at hours	M Group		Control Group		'p'	Significance
	Mean	SD	Mean	SD		
0	75.4	12.7	87.1	11.7	0.0019	**Significant**
2	76	13.7	85.8	9.4	0.0145	**Significant**
4	73.9	13.2	86.6	8.3	0.001	**Significant**
8	72.9	12.3	89	9.8	0.0001	**Significant**
12	73.3	11.1	88.1	9.4	0.0001	**Significant**
16	72	9.8	87.1	7.5	0.0001	**Significant**
20	71.2	10.2	86.6	8.4	0.0001	**Significant**
24	71	9.6	85	6.3	0.0001	**Significant**

Post operative Diastolic BP was 75.4 ± 12.7 in Group - M Vs 87.1 ± 11.7 in control group which is statistically significant p = 0.0019.

Table 13 : Post Operative MAP

Post Op. MAP at hours	Morphine Group		Control Group		'p'	Significance
	Mean	SD	Mean	SD		
0	89	15.7	104	14.3	**0.0012**	**Significant**
2	88	16.1	102	12.4	**0.0049**	**Significant**
4	86	15.9	104	10.1	**0.0002**	**Significant**
8	85	15.3	107	10.9	**0.0001**	**Significant**
12	86	13.9	106	10.8	**0.0001**	**Significant**
16	84	12.4	104	10.1	**0.0001**	**Significant**
20	83	12.4	104	10.3	**0.0001**	**Significant**
24	83	11.7	103	8.8	**0.0001**	**Significant**

The postoperative mean arterial pressure (MAP) is 89 ±15.7 Vs 104 ± 14.3 which is statistically significant (P = 0.0012).

Table 14 : Complications

Complications	Morphine Group		Control Group	
	No.	**%**	**No.**	**%**
Nausea	11	44	9	36
Vomiting	11	44	9	36
Respiratory Depression	3	12	-	-
Pruritis	11	44	5	20
Desaturation	1	4	-	-
Hypotension	3	12	-	-
Bradycardia	2	8	-	-
Total cases with complications	19	76	12	48
Total cases without complications	6	24	13	52
'p'	0.0804 Not significant			

There was no statically significant difference in the complications between the 2 groups. However Nausea & Vomitting was more in the IT Morphine group (11 vs. 9). Desaturation, Pruritis, bradycardia and hypotension was also more in the morphine group. These findings may be clinically relevant although statistical analysis did not reveal any significant difference.

DISCUSSION

The randomized prospective study was conducted at Government General Hospital, Chennai to study the efficacy of intrathecal Morphine 0.5 mg in '1' ml with General anesthesia versus only balanced General anaesthesia followed by multimodal analgesia protocol followed at the institute with respect to intra-operative and post-operative analgesia, Hemodynamics and complications in the two groups.

ANALGESIA

Post operative visual analog score in Group-M was 4.64 vs 5 in group-C. But it was highly significant at 2, 4, 8, 12, 20 Hours and it was not significant at postoperative zero hour, 14, 16, 24 hours. Intrathecal Morphine seems to a superior post-operative analgesia effect.

Kwan As, Lee BB, Brake T showed the median pain free period in prolonged (ie 16-24 hrs) in IT morphine group compared with control group (2-24 hrs). Our study is in concurrence with this study.

Gwirtz KH, **Young JV**, **Byers RS**, **Alley C**, **Levin K**, **Walker SG**, **Stoelting RK** found in their retrospective study intrathecal morphine analgesia was superior for acute postoperative pain in 5969 surgical patients studied at Indiana University Hospital undergoing major urologic, orthopedic, general/ vascular, thoracic, and nonobstetrical gynecologic surgery. The findings in our study are in agreement with this study.

Jean-Michel Devys,Anne Mora, Benoit Plaud et al in their study found IT Morphine 0.4 mg in 60 adult patients undergoing major abdominal surgery produced VAS scores that were lower in the IT morphine group for the first 48 hours, both at rest and during coughing. This is totally in agreement with the findings of this study.

TIME FOR DEMAND ANALGESIA AND DOSES OF RESCUE ANALGESIA

The number of demand analgesic in 24 hours is 1.56 in group-M vs 4.2 in group-C and it is statistically significant (p=0.0002). The total rescue analgesic inj. Fentanyl used in group- M is 1.1 vs. 86 in group-C and it is statistically significant. (p=0.0003).

Jean-Michel Devys,Anne Mora, Benoit Plaud et al studied IT Morphine 0.4 mg in 60 adult patients undergoing major abdominal surgery. Supplemental analgesia consumption was lower and patient satisfaction higher in the IT Morphine group.

Andrew et al studied the efficacy and safety of low dose Intrathecal Morphine for post operative analgesia in children . The time for demand analgesic by patient requiring opioid administration (Parental or oral) was approximately 8 hours. Our study has similar findings establishing the efficacy of IT Morphine for post-operative pain relief.

INTRA-OPERATIVE AND POST-OPERATIVE HAEMODYNAMICS

Hemodynamic parameters including SBP, DBP, MAP, HR, SaO2 were compared both in the intra-operative period and post-operative period. Intra-operatively there was no difference between both the groups. Post-operatively IT Morphine group demonstrated sginigficantly stabler Hemodynamics. This may be related to the more superior and stables pain control that was achieved in this group.

ASK Kwan, BB.Lee, T.Brake et al in their study using 0.2 mg of preservative free morphine 0.2 mg to 2.2 ml of hyperbaric bupivacaine 2.2 ml in patients undergoing hip surgeries demonstrated no alterations in Hemodynamics both in the intra-operative and post-operative period. This asserted the hemodynamic stability of intrathecally used morphine. The findings in our study agree with these conclusions.

POST_OPERATIVE COMPLICATIONS

Nausea & Vomitting was more in the IT Morphine group (11 vs. 9). Desaturation, Pruritis, bradycardia and hypotension was also more in the morphine group. These findings may be clinically relevant although statistical analysis did not reveal any significant difference.

Glynn CG et al [1979] and **Davies GK et al** [1980] reported respiratory depression following spinal morphine. In our study we had 2 patients with

hypoventilation and 1 patient developed desaturation but they were easily manageable by oxygen supplementation.

Reiz and Westberg [1980] and **Yaksh TL** [1981] and **Samii J, Chanin M and Viars P** [1981] reported adverse reactions such as pruritus and urinary retention after intrathecal administration of opioids. Our study recorded Pruritis in patients but urinary retention could not be assessed since all patients continued to have their bladders catheterized during the study period.

Ganesh A, K.M.A. Cucchiaro studied the effect of low dose (4-5μg/kg) intrathecal morphine and found the incidence of Nausea or vomiting, pruritis and urinary retention was 32%, 37% and 6% respectively. The findings in our study are in concurrence with these studies.

SUMMARY

The study was conducted at Government General Hospital, Chennai on fifty patients to compare the effect of IT morphine (0.5 mg) for providing post-operative analgesia in patients undergoing major laprotomies. The summary of the findings include

1. Intrathecal Morphine produced better post-operative analgesia as shown by lower VAS scores.

2. Intrathecal Morphine group demonstrated lesser amounts of analgesic and rescue analgesic requirements during the post-operative period.

3. Intrathecal Morphine group of patients has better sedation as shown by better scores on the Ramsay scale.

4. Intrathecal Morphine produced better hemodynamic stability in the post-operative period and also was associated with lower heart rates.

5. Intrathecal Morphine produced more side effects in the form of nausea, vomiting, hypotension, bradycardia and hypotension. Although not statistically significant these findings seem to be clinically relevant. A larger sample of study may have revealed statistical significance.

6. All the side effects produced by IT Morphine were easily manageable and did not contribute to any increase in mortality or morbidity.

7. IT Morphine did not seem to produce any significant changes in the Hemodynamics or management of the patient during the intra-operative period. This may be related to the lag time for the rostral spread of the drug.

8. IT Morphine is a good substitute or adjunct to various modalities used to offer analgesia during the post-operative period in patients undergoing major laprotomies

9. IT Morphine does not require any complex procedures and or equipment for administration

10. IT Morphine is a cost effective adjunct and alternative to the various modalities available to provide pain relief during the post- operative period.

CONCLUSION

Preservative free morphine 0.5 mg administered intrathecally in patients undergoing laparotomies under general anesthesia

Provides effective analgesia during the first 24 hours of the post-operative period.

It decreases the requirement of rescue analgesics during the post-operative period.

It is associated with stable Hemodynamics and better levels of sedation.

It is associated with increased adverse effects but these are easily manageable by simple measures.

INTRA OPERATIVE MEAN ARTERIAL PRESSURE

MORPHINE GROUP

No	INTRA OPERATIVE MEAN ARTERIAL PRESSURE AT MINUTES												
	0	**15**	**30**	**45**	**60**	**75**	**90**	**105**	**120**	**135**	**150**	**165**	**180**
1	83	84	90	84	85	82	81	86	88	87	86	80	79
2	97	60	93	95	103	101	101	99	101	103	99	97	100
3	97	69	85	83	87	72	85	92	81	84	85	88	82
4	94	63	97	105	98	91	91	94	97	95	95	90	86
5	78	57	81	76	85	82	78	74	71	76	77	81	82
6	109	67	113	116	107	101	101	99	104	96	101	99	83
7	113	63	88	87	83	90	91	91	94	99	95	91	89
8	95	59	81	81	83	93	83	84	101	104	104	105	104
9	89	87	118	117	75	72	70	85	84	86	89	86	73
10	90	77	90	98	97	97	90	97	98	93	83	80	81
11	80	52	79	95	103	95	88	97	96	89	91	93	92
12	119	67	81	97	97	101	103	98	99	98	100	90	113
13	96	70	81	91	88	97	89	87	84	83	88	81	83
14	89	54	115	117	79	79	90	97	97	100	93	97	101
15	82	55	114	97	105	103	120	103	118	111	105	88	83
16	103	71	97	92	97	98	93	91	77	87	91	93	96
17	94	65	73	81	83	109	87	101	88	84	92	95	99
18	97	70	87	91	90	89	94	87	99	95	95	92	97
19	95	65	89	93	110	92	84	89	95	96	90	93	96
20	97	65	84	80	97	99	96	88	89	89	89	86	92
21	85	89	87	83	81	85	81	81	81	94	100	100	90
22	83	53	93	87	80	81	73	82	70	90	80	72	78
23	107	63	83	88	90	93	81	73	70	83	77	85	86
24	97	73	97	93	89	88	87	91	98	100	107	101	100
25	97	67	113	97	94	93	89	83	73	87	92	97	99

INTRA OPERATIVE MEAN ARTERIAL PRESSURE

CONTROL GROUP

No	INTRA OPERATIVE MEAN ARTERIAL PRESSURE AT MINUTES												
	0	**15**	**30**	**45**	**60**	**75**	**90**	**105**	**120**	**135**	**150**	**165**	**180**
1	117	71	98	107	107	109	107	110	103	103	105	100	95
2	99	77	100	97	102	93	99	111	91	104	87	91	94
3	99	72	91	81	81	87	91	91	91	93	97	98	99
4	95	67	80	87	95	95	97	96	86	94	93	93	96
5	120	79	103	103	106	111	113	112	100	107	110	109	103
6	83	61	87	79	82	84	84	83	81	80	79	71	77
7	83	47	86	70	83	76	86	83	79	74	73	71	73
8	103	71	120	103	99	97	99	97	93	93	93	91	90
9	77	63	84	81	83	83	84	84	79	79	81	83	80
10	91	82	93	91	109	107	105	103	98	94	95	92	89
11	120	69	87	101	96	103	91	88	101	107	101	107	90
12	96	59	90	83	105	97	100	95	97	96	92	95	97
13	99	58	105	90	101	106	103	90	100	87	98	102	111
14	95	79	96	99	105	108	107	105	97	100	92	78	78
15	83	53	77	83	80	83	90	89	90	94	91	87	85
16	95	57	79	84	91	83	83	83	81	95	97	91	91
17	97	77	105	106	82	97	83	76	77	77	80	82	79
18	97	67	99	102	105	104	97	96	101	103	103	105	98
19	93	64	83	87	87	83	93	89	89	85	90	84	95
20	97	83	98	112	109	105	104	100	112	114	112	102	101
21	97	53	99	107	91	94	103	99	94	107	98	101	110
22	77	60	83	76	85	97	82	83	83	81	80	77	83
23	93	57	97	91	104	97	83	100	107	97	111	97	91
24	90	63	90	79	91	84	92	88	85	85	93	90	95
25	126	102	121	121	121	95	101	87	89	100	99	97	96

POST OPERATIVE MEAN ARTERIAL PRESSURE

MORPHINE GROUP

No	INTRA OPERATIVE MEAN ARTERIAL PRESSURE AT HOURS							
	0	**2**	**4**	**8**	**12**	**16**	**20**	**24**
1	89	95	87	93	92	80	80	80
2	93	70	71	70	74	74	71	73
3	109	108	105	114	112	97	99	97
4	101	97	86	67	73	73	80	80
5	80	73	73	74	76	76	73	73
6	104	107	107	101	97	98	100	93
7	96	97	98	97	98	97	93	93
8	70	71	70	70	71	70	70	71
9	113	117	110	107	108	105	105	109
10	80	90	70	77	80	95	81	81
11	91	87	87	90	84	77	78	77
12	70	71	71	70	70	70	71	71
13	80	79	79	80	81	80	80	80
14	73	70	71	71	73	77	78	75
15	107	108	105	99	102	99	97	95
16	75	77	70	77	78	76	74	78
17	72	73	72	70	71	71	70	70
18	77	75	75	68	71	75	67	69
19	120	115	117	107	107	107	107	105
20	80	80	80	79	79	80	79	79
21	105	107	108	96	97	98	101	99
22	71	70	70	70	70	71	70	70
23	93	89	92	93	95	83	83	83
24	107	108	107	108	104	101	93	93
25	70	77	77	75	79	80	80	80

POST OPERATIVE MEAN ARTERIAL PRESSURE

CONTROL GROUP

No	INTRA OPERATIVE MEAN ARTERIAL PRESSURE AT HOURS							
	0	**2**	**4**	**8**	**12**	**16**	**20**	**24**
1	98	95	97	96	96	99	99	95
2	83	79	96	97	98	100	91	97
3	76	83	89	83	83	83	83	90
4	107	107	99	108	103	103	100	100
5	101	107	105	107	101	104	104	101
6	116	95	111	126	123	123	119	110
7	117	107	106	108	113	113	120	117
8	107	107	101	117	117	115	113	108
9	115	101	101	101	96	99	87	88
10	103	105	112	115	114	107	106	98
11	101	94	93	93	97	89	99	93
12	103	100	99	100	94	95	93	98
13	123	122	121	127	117	114	109	107
14	117	120	115	111	114	111	110	119
15	82	98	98	98	110	101	99	99
16	107	104	112	113	108	108	123	95
17	115	113	111	108	106	99	102	101
18	113	104	101	97	100	93	97	99
19	70	76	83	99	105	107	99	99
20	107	107	108	121	92	95	105	105
21	95	93	90	99	97	93	98	95
22	100	90	108	103	100	105	110	106
23	107	110	121	113	122	117	113	115
24	127	122	117	115	117	118	110	115
25	118	117	116	119	124	116	119	115

COMPLICATIONS MASTER CHART

MORPHINE GROUP

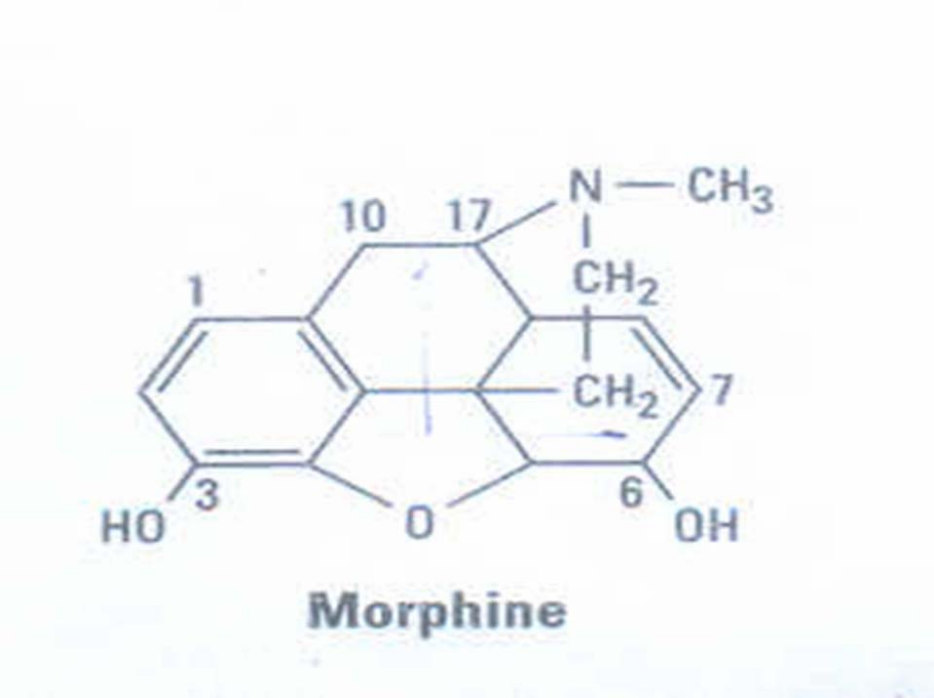
No.	TIME FOR 1st PT ANALGESIA DEMAND	NO OF ANALGESIA DEMAND IN 24 HOURS	TOTAL TRAMADOL USED IN 24 HOURS	TOTAL NSAID USED IN 24 HOURS	FENTANYL	Nausea	Vomiting	Respiratory	Pruritis	Desaturation	Hypotension	bradycardia
1	24	0		0	0	Yes	Yes	No	No	No	No	No
2	24	0		0	0	No	No	No	Yes	No	No	No
3	0	2		1	1	No	No	No	Yes	No	No	No
4	24	0		0	0	Yes	Yes	No	Yes	No	Yes	No
5	24	0		0	0	No	No	No	Yes	No	No	No
6	0	2		1	1	Yes	Yes	No	No	No	No	No
7	0	5		1	4	No	No	No	No	No	No	No
8	10	2		1	1	No	No	No	Yes	No	No	Yes
9	0	3		1	2	No	No	Yes	No	No	No	No
10	24	0		0	0	No	No	No	No	No	No	No
11	24	0		0	0	Yes	Yes	No	Yes	No	No	No
12	24	0		0	0	No	No	No	No	No	No	No
13	24	0		0	0	No	No	No	No	No	No	No
14	24	0		0	0	Yes	Yes	No	Yes	No	No	No
15	0	6		1	5	Yes	Yes	No	No	No	No	No
16	0	4		1	3	No	Yes	Yes	No	No	Yes	Yes
17	24	0		0	0	No	No	No	No	No	No	No
18	24	0		0	0	No	No	No	Yes	No	No	No
19	0	5		1	4	Yes	Yes	No	No	No	Yes	No
20	24	0		0	0	Yes	Yes	No	No	No	No	No
21	0	8		1	7	No	No	No	Yes	No	No	No
22	24	0		0	0	No	No	No	Yes	No	No	No
23	0	1		1	0	No	No	No	No	No	No	No
24	0	1		1	0	Yes	Yes	Yes	No	No	No	No
25	24	0		0	0	Yes	Yes	No	Yes	No	No	No

NSAID - Inj. Diclofenac 75 mg

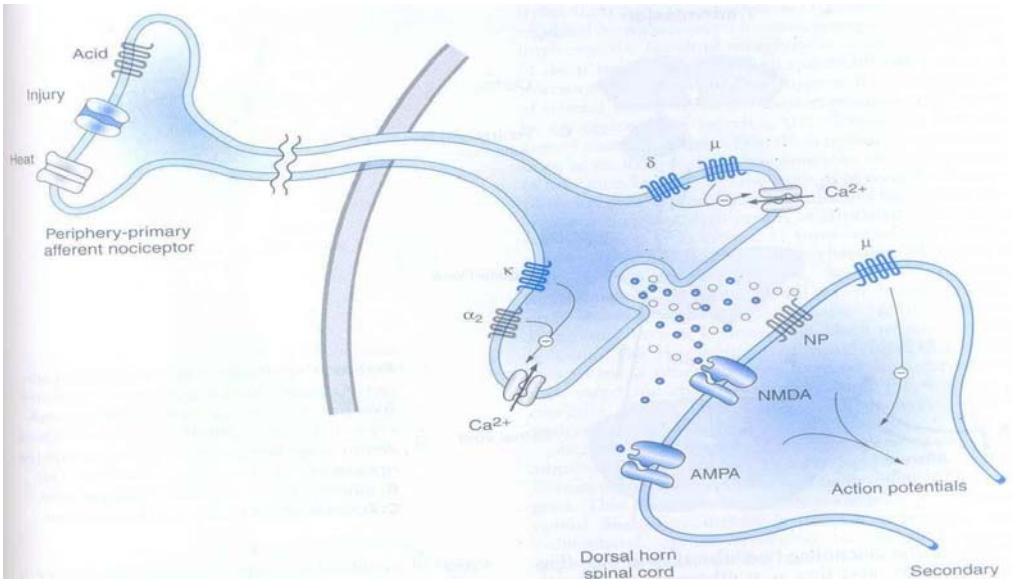
COMPLICATIONS MASTER CHART

CONTROL GROUP

No.	TIME FOR 1st PT ANALGESIA DEMAND	NO OF ANALGESIA DEMAND IN 24 HOURS	TOTAL TRAMADOL USED IN 24 HOURS	TOTAL NSAID USED IN 24 HOURS	RESCUE FENTANYL (µg)	Nausea	Vomiting	Respiratory	Pruritis	Desaturation	Hypotension	bradycardia
1	0	7	DT		150	No	No	No	No	No	No	No
2	0	7	DT		150	No	No	No	No	No	No	No
3	0	3	DT		50	Yes	Yes	No	Yes	No	No	No
4	0	5	DT		100	Yes	Yes	No	Yes	No	No	No
5	2	1	DT		0	No	No	No	No	No	No	No
6	2	1	DT		0	Yes	Yes	No	No	No	No	No
7	2	1	DT		0	No	No	No	Yes	No	No	No
8	2	1	DT		0	No	No	No	No	No	No	No
9	0	8	DT		175	No	No	No	No	No	No	No
10	0	7	DT		150	No	No	No	No	No	No	No
11	2	4	DT		75	No	No	No	No	No	No	No
12	0	7	DT		150	No	No	No	No	No	No	No
13	2	6	DT		125	Yes	Yes	No	No	No	No	No
14	0	8	DT		175	No	No	No	No	No	No	No
15	2	1	DT		0	No	No	No	Yes	No	No	No
16	2	3	DT		50	No	No	No	No	No	No	No
17	0	6	DT		125	Yes	Yes	No	No	No	No	No
18	2	1	DT		0	Yes	Yes	No	No	No	No	No
19	0	7	DT		150	No	No	No	Yes	No	No	No
20	2	1	DT		0	No	No	No	No	No	No	No
21	2	1	DT		0	Yes	Yes	No	No	No	No	No
22	0	7	DT		150	Yes	Yes	No	No	No	No	No
23	0	9	DT		200	Yes	Yes	No	No	No	No	No
24	2	2	DT		25	No	No	No	No	No	No	No
25	0	1	DT		150	No	No	No	No	No	No	No

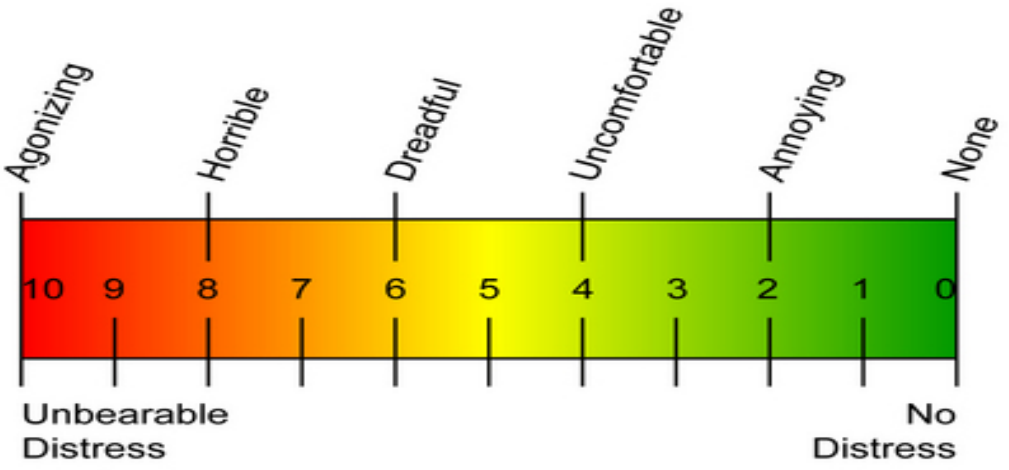


Morphine



SPINAL SITE OF ACTION OF OPIOIDS

VISUAL ANALOG SCALE



INSTITUTIONAL ETHICAL COMMITTEE

GOVERNMENT GENERAL HOSPITAL & MADRAS MEDICAL COLLEGE,
CHENNAI-600 003.

Telephone: 044-2530 5000
Fax : 044 - 25305113

K.Dis.No.16328 P & D3/Ethies/Dean/GGH/08 Dated: 8.9.2008

Title of the work : "To compare the efficacy of intrathecal Morphine with multimodal analgesia for post op analgesia in patients undergoing laparotomies under GA"

Principal Investigator :

Department : Anaesthesiology, MMC & GuH Ch-3.

The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 10th September 2008 at 2 P.M in Government General Hospital, Deans, Chamber, Chennai-3.

The members of the Committee, the Secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

The principal investigator and their term are directed to adhere the guidelines given below:

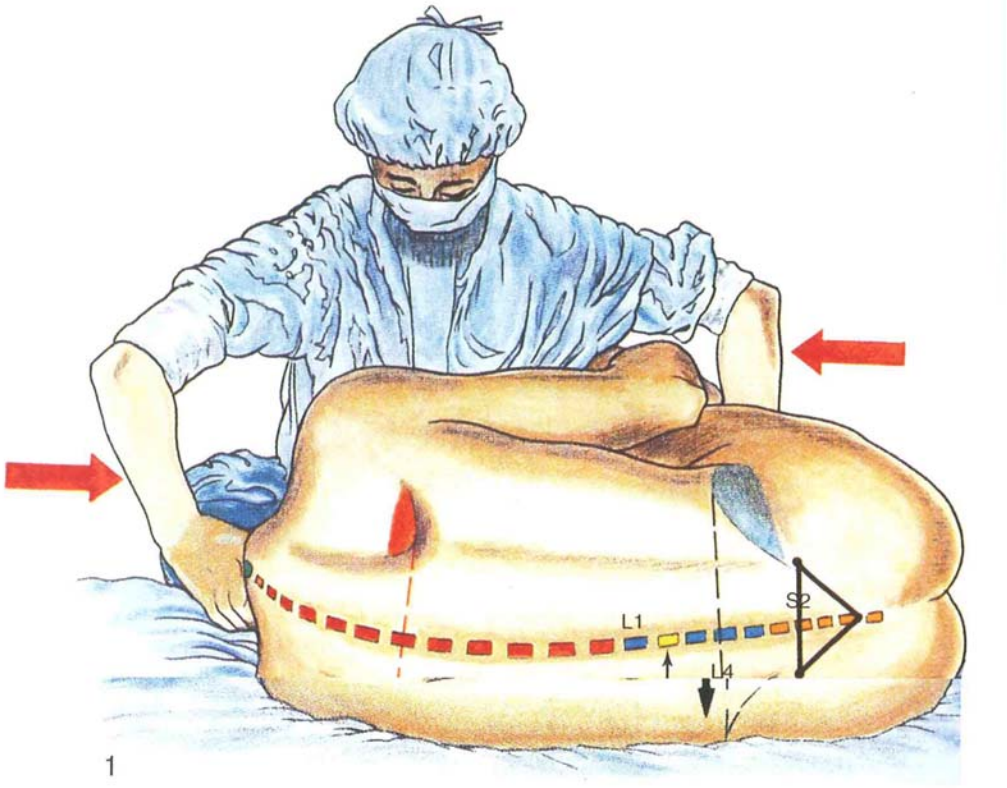
1. You should get detailed informed consent from the patients/participants and maintain confidentiality.
2. You should carry out the work without detrimental to regular activities as well as without extra expenditure to the Institution or Government.
3. You should inform the IEC in case of any change of study procedure, site and investigation or guide.
4. You should not deviate form the area of the work for which I applied for ethical clearance
5. You should inform the IEC immediately, in case of any adverse events or serious adverse reactions.
6. You should abide to the rules and regulations of the institution(s)
7. You should complete the work within the specific period and if any extension of time is required, you should apply for permission again and do the work.
8. You should submit the summary of the work to the ethical committee on completion of the work.
9. You should not claim funds from the Institution while doing the work or on completion.
10. You should understand that the members of IEC have the right to monitor the work with prior intimation.

SECRETARY
IEC, GGH,CHENNAI

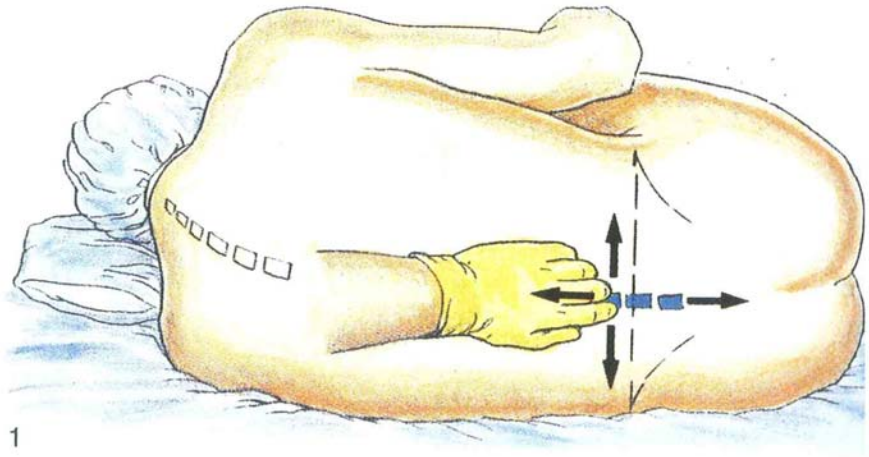
CHAIRMAN
IEC, GGH,CHENNAI

DEAN
GGH &MMC, CHENNAI

Rkm.5.9(2)

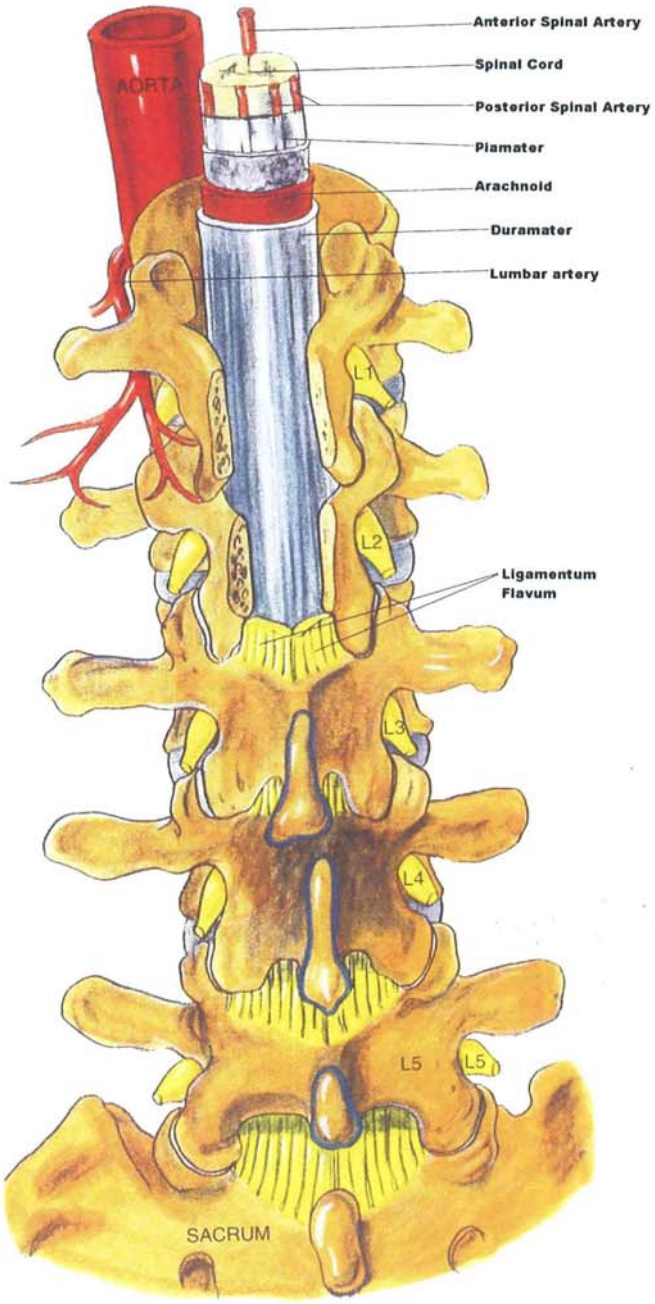


1



1

SPINAL ANAESTHESIA TECHNIQUE



SPINAL CORD ANATOMY

PROFORMA

NAME :

AGE / SEX:

DIAGNOSIS :

SURGERY :

PRE OP ASSESMENT

1.AIRWAY :

2,BACK LANDMARKS

3.COMORBID ILLNESS

ASA STATUS :

HEIGHT :

WEIGHT :

BMI :

INVESTIGATIONS :

Hb.&PCV :

BT , CT

BLOOD SUGAR

UREA

SERUM CREATININE

ELECTROLYTES

PREMED:

IV ACCESS: 18 G

PRELOAD FLUID VOLUME

RL / NS	500ML

SUBARACHNOID BLOCK

SPACE	NEEDLE	SIZE	APPROACH
L 3,4	QUINCKIE	25 G	MEDIAN

GROUP	MORPHINE	CONTROL	TOTAL VOLUME
	0.5mg	NONE	1cc

GENERAL ANAESTHESIA :

Premedication: inj. Glycopyrrolate 0.2 mg + Fentanyl 2µg / Kg

Pre oxygenation with 100% O2 for 3 min.

Induction : Inj. Thiopentone 5mg/Kg + suxamethonium 2mg /kg.

Intubation with 8 /8.5 CETT orally.

Maintenance N2O –O2 :150

Relaxant : Vecuronium 0.12 mg /kg

Reversal : Inj. Neostigmine 2.5 mg + Glycopyrrolate 0.4 mg.

Extubation :

Intra op vitals:

TIME	**0**	**15 min**	**30 min**	**45 min**	**1 hr**	**1.15**	**1.30**	**1.45**	**2**	**2.15**	**2.30**	**2.45**	**3**
PR													
BP													
SPO2													

POST OP : Patient shifted to PACU for observation.

Recovery :

TIME	0	2	4	6	8	10	12	16	20	24
VAS										
RSS										
PR										
SPO2										
BP										

Complications	YES /NO	Interventions Needed
1. PRURITIS 2. NAUSEA 3. VOMITING 4. RESPIRATORY DEPRESION 5. RETENTION OF URINE		

BIBLIOGRAPHY

1. **Behar M *et al*.** Epidural morphine in the treatment of pain. *Lancet* 1979; **1:** 527-529.

2. **Wang JK, Nauss LA, Thomas JE.** Pain relief by intrathecally applied morphine in man. *Anesthesiology* 1979; **50:** 149-151.

3. **Kalso E.** Effects of intrathecal morphine injected with bupivacaine on pain after orthopaedic surgery. *Br J Anaesthiol* 1983; **55:** 415-422.

4. **Nordberg G *et al*.** Pharmacokinetic aspects of intrathecal morphine analgesia. *Anesthesiology* 1984; **60:** 448-454.

5. **Chadwick HS, Ready LB.** Intrathecal and epidural morphine sulfate for post cesarean analgesia: a clinical comparison. *Anesthesiology* 1988; **67:** 137-143.

6. **Abboud TK *et al*.** Mini-dose intrathecal morphine for the relief of post-cesarean section pain. *Anesth Analg* 1988; **67:** 137-143.

7. **Abouleish E *et al*.** Combined intrathecal morphine and bupivacaine for cesarean section. *Anesth Analg* 1988; **67:** 370-374.

8. **Kirson LE, Goldman JM, Slover RB.** Low-dose intrathecal morphine for postoperative pain control in patients undergoing transurethral resection of the prostate. *Anesthesiology* 1989; **71:** 192-195.

9. **Gustafsson LL, Schildt B, Jacobsen K.** Adverse effects of extradural and intrathecal opiates: report of a nationwide survey in Sweden. *Br J Anaesthiol* 1982; **54:** 479-486.

10. **Gwirtz KH *et al*.** The safety and efficacy of intrathecal opioid analgesia for acute postoperative pain: seven years' experience with 5969 surgical patients at Indiana University hospital. *Anesth Analg* 1999; **88:** 599-604.

11. **Walsh PC.** Radical retropubic prostatectomy. In: Walsh PC, Retik AB, Vaughan ED, Wein AJ (eds) *Campbell's Urology* 7th edn WB Saunders: Philadelphia, 1998, pp 2565-2588.

12. **Fowler FJ Jr *et al.*** Effect of radical prostatectomy for prostate cancer on patient quality of life: results from a Medicare survey. *Urology* 1995; **45:** 1007-1015.

13. **Litwin MS, Shpall AI, Dorey F.** Patient satisfaction with short stays for radical prostatectomy. *Urology* 1997; **49:** 898-906.

14. **Worwag E, Chodak GW.** Overnight hospitalization after radical prostatectomy: the impact of two clinical pathways on patient satisfaction, length of hospitalization, and morbidity. *Anesth Analg* 1998; **87:** 62-67.

15. **Palmer JS *et al.*** Same day surgery for radical retropubic prostatectomy: is it an attainable goal? *Urology* 1996; **47:** 23-28.

16. **Shir Y *et al.*** Intraoperative blood loss during radical retropubic prostatectomy: epidural versus general anesthesia. *Urology* 1995; **45:** 993-999.

17. **Eastham JA, Scardino PT.** Radical prostatectomy. In: Walsh PC, Retik AB, Vaughan ED, Wein AJ (eds) *Campbell's Urology* 7th edn WB Saunders: Philadelphia, 1998, pp 2547-2564.

18. **Allano C *et al.*** Low dose spinal morphine for postop analgesia on surgical wards. *Br J Anethesiol* 1999; **82:** 189.

19. **Chaney M.** Side effects of intrathecal and epidural opioids (Review). *Can J Anesth* 1995; **42:** 891-903.

20. **Johnson A *et al.*** Influence of postoperative naloxone infusion on respiration and pain relief after intrathecal morphine. *Reg Anesth* 1988; **13:** 146-151.

21. **Stoelting RK.** Intrathecal morphine: an underused combination for postoperative pain management. *Anesth Analg* 1989; **68:** 707-709.

22. **Watts RW.** A five-year prospective analysis of the efficacy, safety and morbidity of epidural anaesthesia performed by a general practitioner anaesthetist in an isolated rural hospital. *Anaesth Intensive Care* 1992; **20:** 348-353.

23. **Gerig HJ, Kern F.** Success and failure rate in peridural anesthesia. A 1-year study. *Reg Anaesth* 1985; **8:** 25-32.

24. **Gerancher JC, Liu SS.** Complications of neuraxial (spinal/epidural/caudal) anesthesia. In: Benumof JL, Saidman LJ (eds) *Anesthesia and Perioperative Complications* 2nd edn Mosby: St. Louis, MO, 1999, pp 50-65.

25. **Klein EA *et al*.** maintaining quality of care and patient satisfaction with radical prostatectomy in the era of cost containment. *Urology* 1996; **48:** 269-276.

26. **Gottschalk A *et al*.** Preemptive epidural analgesia and recovery from radical prostatectomy. *JAMA* 1998; **279:** 1076-1082.

27. **Brownridge P.** Epidural and subarachnoid analgesia for elective Caesarean section. *Anesthesia* 1986; **36**: 70

28. **Sauter K, Kaufman HH, Bloomfield SM, *et al***. Treatment of high-dose intrathecal morphine overdose. *J Neurosurg* 1994; **81**: 143–6

29. **Groudine SB, Cresanti-Dakins C, Lumb PD**. Succesful treatment of a massive intrathecal morphine overdose. *Anesthesiology* 1995; **82**: 292–5

30. **Perrot G, Muller A, Laugner B.** Accidental overdose of intrathecal morphine. Treatment with intravenous naloxone alone. *Ann Fr Anesth Reanim* 1983; **2**: 412–14

31. **Pomonis SP, Economacos G, Costopanajiocoy SP.** Overdose of intrathecal morphine. *Anesthesia* 1986; **41**: 670

32. **Kaiser KG, Bainton CR.** Treatment of intrathecal morphine overdose by aspiration of cerbrospinal fluid. *Anesth Analg* 1987; **66**: 475–7

33. **Kreitzer JM, Kirshenbaum LP, Eisenkraft JB.** Safety of PCA devices. *Anesthesiology* 1989; **70**: 881

34. **Dahl JB, Jacobsen JB.** Accidental epidural narcotic overdose. *Anesth Analg* 1990; **70**: 321–2

35. **Parkinson SK, Bailey SL, Little WL, Mueller JB.** Myoclonic seizure activity with chronic high-dose spinal opioid administration. *Anesthesiology* 1990; **72**: 743–5

36. **Bruera E.** Narcotic-induced pulmonary edema. *J Pain Symptom Management* 1990; **5**: 55–8

37. **Flacke JW, Flacke WE, Williams GD**. Acute pulmonary edema following naloxone reversal of high-dose morphine anesthesia. *Anesthesiology* 1977; **47**: 376–8

38. **Shohami E, Evron S.** Intrathecal morphine induces myoclonic seizures in the rat. *Acta Pharmacol Toxicol* 1985; **56**: 50–4

39. **Bailey PL, Lu JK, Orr JA, *et al*.** Effects of intrathecal morphine on the ventilatory response to hypoxia. *N Engl J Med* 2000; **343**: 1228–341.

40. **Albense J, Durbec O., Viviand, X et al.** Sufentanil Increases intracranial pressure in patients with head trauma. Anaesthesiology 1993; 79 : 493 - 497.

41. **Behar, M., Oshwant, D. Magora, F., Dvidson, JT.** Epidural morphine in the treatment of pain, lancet 1979 ; 50 : 149 - 151.

42. **Bromage, PR, Camporesi, EM, Durant, PAC, Nielsen, CH.** respiratory side effects of epidural morphine. Anesth Analg 1982 ; 61 : 490 - 495.

43. **Cousins, M.J. and Mather, L.E.** Intrathecal and epidural administration of opioids. Anesthesiology, 1984: 61 : 270 - 310.

45. **Crawford, J.S.** Site of action of intrathecal morphine, Br. Med J. 1980; 281 : 660.

46. **Davies, GK, Tholhurst - Cleaver, CL, James TL.** Respiratory depression after intrathecal narcotics. Anaesthesia, 1980; 35 : 1080 - 1083.

47. **De Belle B, Breen TW;** Intrathecal opioids for combined spinal epidural analgesia during labor; CNS Drugs 2003; 17(12) : 889 - 904.

48. **Glynn, CJ, Maher, LG, Cousins, MJ, Wilson, PR, Graham, JR.** Spinal narcotics and respiratory depression. Lancet 1979 ; 2 : 256 - 257.

49. **Goodarzi M, Narasimhan, RR.** The effect of large-dose intrathecal opioids on the autonomic nervous system. Anesthe analg 1999; 89 : 378.

50. **Stoelting, RK.** Intrathecal Morphine - An underused combination for postoperative pain management. Anesthesia and Analgesia 1989; 68 : 707 - 709.

51. **Wang, JK, Nauss, LA and Thomas JE.** Pain relief by intrathecally applied morphine in man. Anesthesiology 1979; 50 : 149 - 151.

52. **Willer, JC and Bussel B.** Evidence for a direct spinal mechanism in morphine - induced inhibition of nociceptive reflexes in human. Brain Research 1980 : 187 : 212 - 215.

53. **Yaksh, TL and Rudy, TA.** Analgesia mediated by a direct spinal action of narcotics. Science 1976 : 192 : 1357 - 8.

54. **Yaksh, TL.,** Spinal opiate analgesia. Characteristic and principles of action. Pain 1981; 11 : 292 - 346.

55. **Abboud TK, Dror A, Mosaad P, et al.** Mini-dose intrathecal morphine for the relief of post cesaean section pain : safety, efficacy, and ventilatory responses to carbon dioxide. Aneth Analg 1988; 67: 137-43.

56. **Motamed C, Bouaziz H, Franco D, Benhamou D.** Analgesic effect of low-dose intrathecal morphine and bupivacaine in laparoscop ic cholecystectomy. 2000; 55: 118-24.

57. **Sarma VJ, Bostrom UV.** Intrathecal morphine for the relief of post hysterectomy pain - a double-blind, dose-response study. Acta Anaesthesiol Scand 1993; 37: 223-7.

58. **Gray JR, Fromme GA, nauss La, Wang JK, Ilstrup DM** intrathecal morphine for post thoracotomy pain. Anesth Analg 1986; 65: 873-6.

59. **Gall O, Aubineau JV, Berniere J, Desjeux L, Murat I.** Analgesic effect of low-dose intrathecal morphine after spinal fusion in children. Anesthesiology 2001; 94: 447-52.

60. **Swart M, Sewell J, Thomas D.** Intrathecal morphine for caesarean section: an assessment of pain relief, satisfaction and side-effects. Anaesthesia 1997; 52: 373-81.

61. **Gwirtz KH, Young JV, Byers RS, et al.** The safety and efficacy of intrathecal morphine acute postoperative pain: seven years' experience with 5969 surgical patients at Indiana University Hospital. Anesth Analg 1999; 88: 599-604.

62. **Yaksh TL.** Pharmacology and mechanisms of opioid analgesic activity. In: Yaksh TL, Lynch CL, Zapol WM, Maze M, Biebuyck JF, Saidman LJ (Eds.) Anesthesia: Biologic Foundations. Philadelphia: Lippincott-Raven; 1997: 921-35.

63. **Clergue F, Montembault C, Despierres O, Ghesquiere F, Harari A, Viars P.** Respiratory effects of intrathecal morphine after upper abdominal surgery. Anesthesiology 1984; 61: 677-85.

64. **Bailey PL, Lu JK, Pace NL, et al.** Effects of intrathecal morphine on the ventilatory response to hypoxia. N Engl J Med 2000; 343: 1228-34.

65. **Cousins MJ, Mather LE.** intrathecal morphine and epidural administration of opioids. Anesthesiology 1984; 61: 276-310.

66. The use of intrathecal morphine for postoperative pain relief after liver resection: a comparison with epidural. **Anesth. Analg.,** April 1, 2006; 102(4): 1157-1163.